ISRS
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SRS/SRT IN MANAGEMENT OF INTRACRANIAL METASTASES, PARENCHYMAL BRAIN TUMORS, GENITOURINARY, GYNECOLOGICAL, AND ABDOMINAL CANCERS; MEDICAL PHYSICS AND IMAGING FOR RADIOSURGERY

DECEMBER 18-20, 2023; İSTANBUL, TÜRKİYE

Irradiation of Gastrointestinal Cancers

Alexandr Pankratov

Centre of Oncology and Radiotherapy "PET-Technology Balashikha" Ltd. ,
Balashikha, Moscow Region, Russia

Istanbul, 18-21 of December 2023

Cancers of the Digestive System

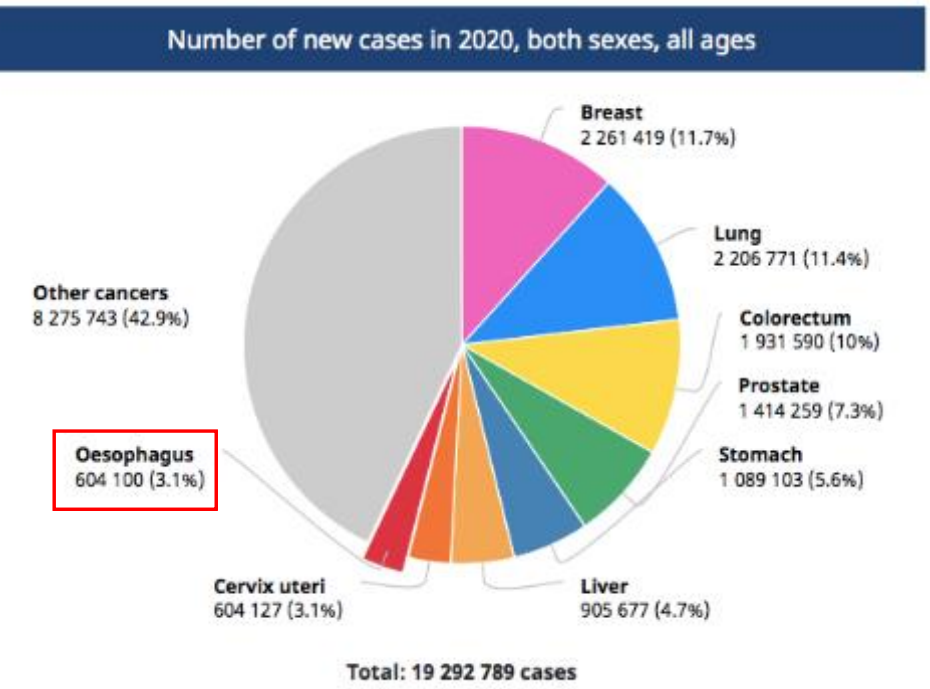
- **Esophageal**
- **Stomach**
- Pancreas
- Liver malignancy (Hepatocellular Ca, mts)
- Gall blader
- Bile Duct
- **Rectal**
- Anal

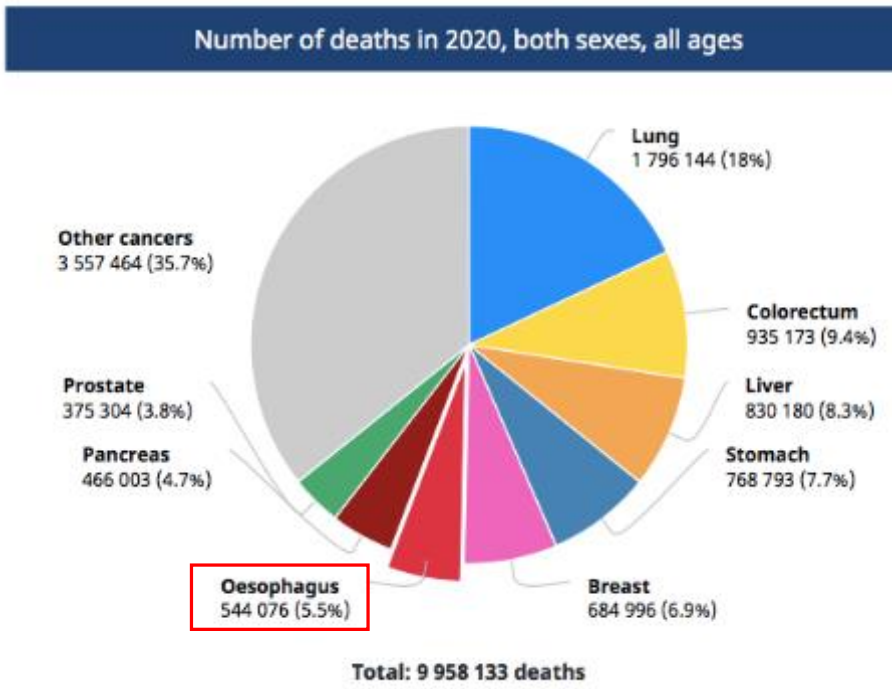
Esophageal Cancer

Esophageal cancer is an extremely aggressive, lethal malignancy that is increasing in incidence worldwide, 5-10 per 100,000

Oesophagus

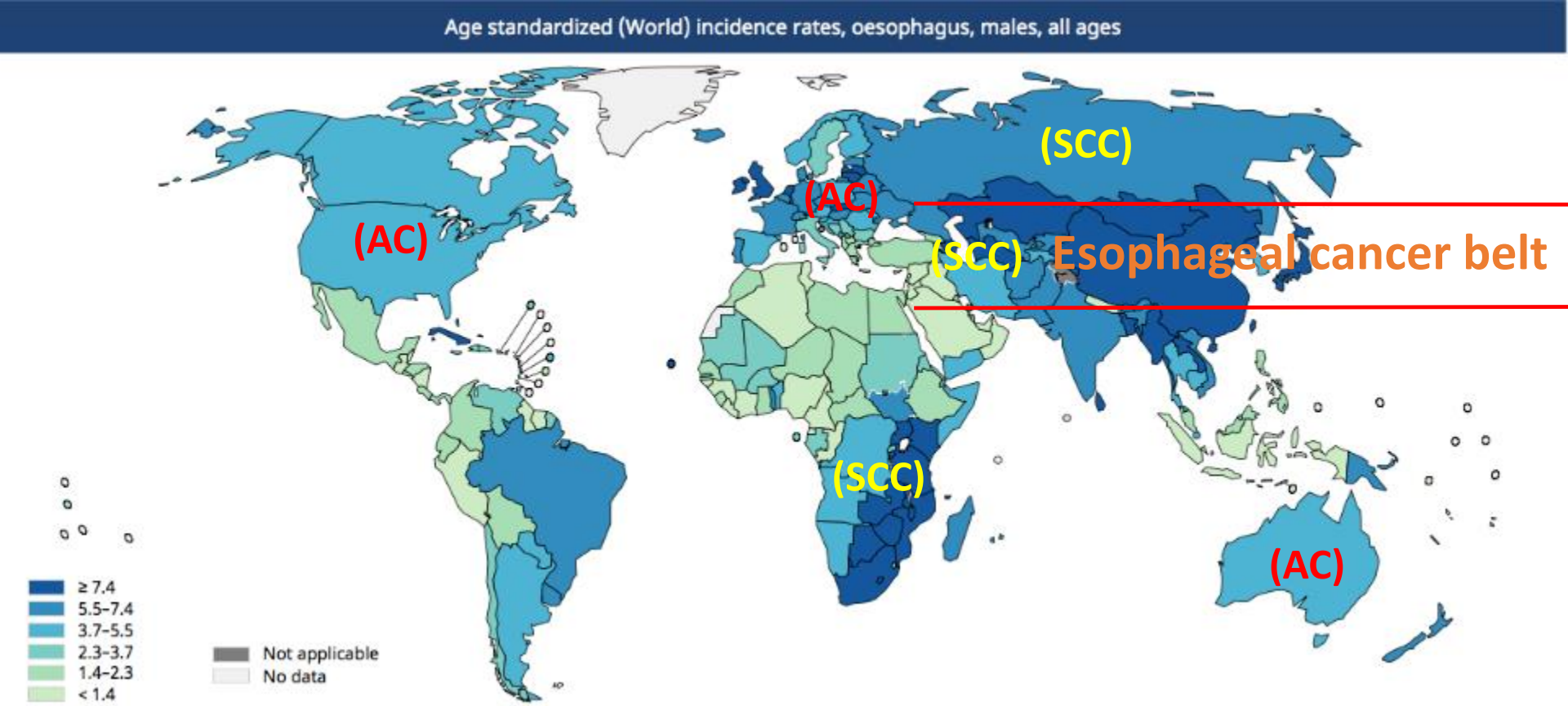
Source: Globocan 2020





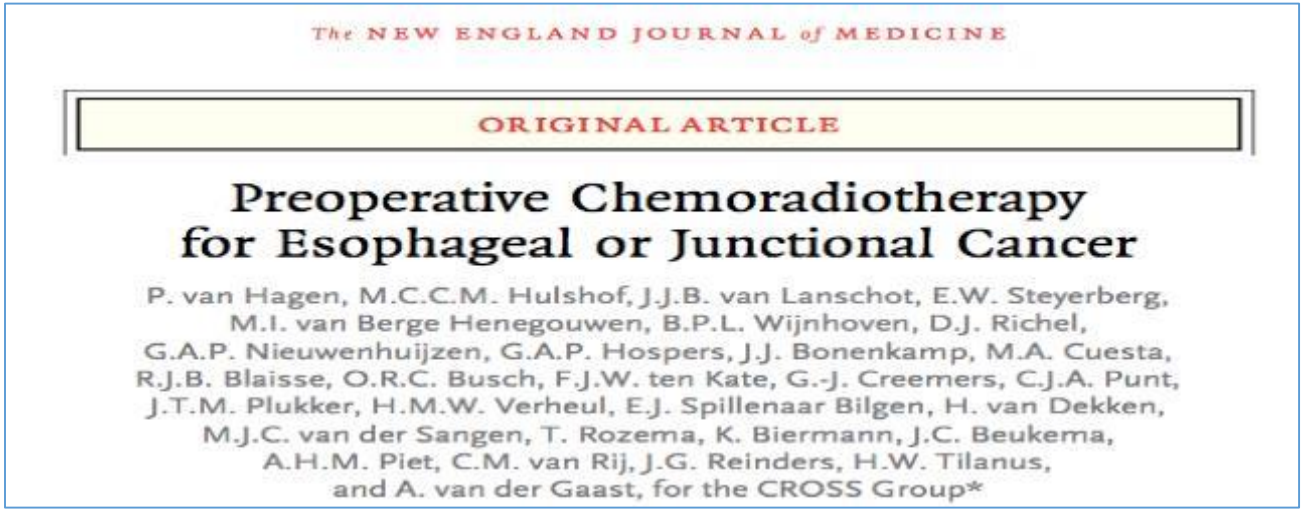
Prevalence – 8th position,

Mortality – 6th among other types of cancer


Age standardized (World) incidence rates, oesophagus, males, all ages
(SCC)
(AC)
(AC)
(SCC)
Esophageal cancer belt
(SCC)
(AC)
≥ 7.4
5.5–7.4
3.7–5.5
2.3–3.7
1.4–2.3
< 1.4
Not applicable
No data
World Health Organization

Squamous cell carcinoma 28 - 90%
Adenocarcinoma 10% - 70%

Neoadjuvant chemoradiotherapy followed by surgery is the standard treatment for patients with esophageal cancer.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preoperative Chemoradiotherapy for Esophageal or Junctional Cancer

P. van Hagen, M.C.C.M. Hulshof, J.J.B. van Lanschot, E.W. Steyerberg, M.I. van Berge Henegouwen, B.P.L. Wijnhoven, D.J. Richel, G.A.P. Nieuwenhuijzen, G.A.P. Hospers, J.J. Bonenkamp, M.A. Cuesta, R.J.B. Blaisse, O.R.C. Busch, F.J.W. ten Kate, G.-J. Creemers, C.J.A. Punt, J.T.M. Plukker, H.M.W. Verheul, E.J. Spillenaar Bilgen, H. van Dekken, M.J.C. van der Sangen, T. Rozema, K. Biermann, J.C. Beukema, A.H.M. Piet, C.M. van Rij, J.G. Reinders, H.W. Tilanus, and A. van der Gaast, for the CROSS Group*

368 patients
adenocarcinoma 75%
squamous-cell carcinoma 23%
large-cell undifferentiated carcinoma 2%

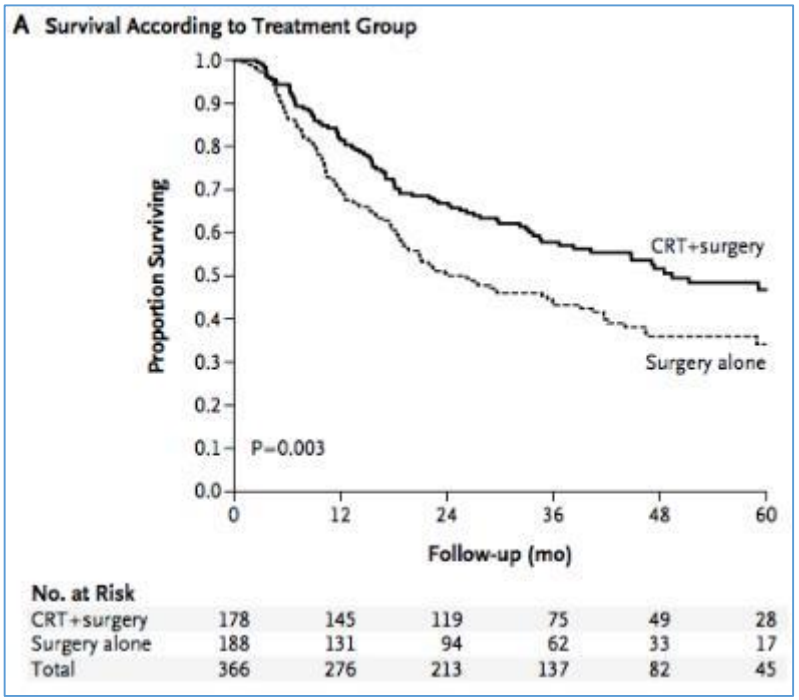
CRT followed by Surgery 178
Surgery alone 188

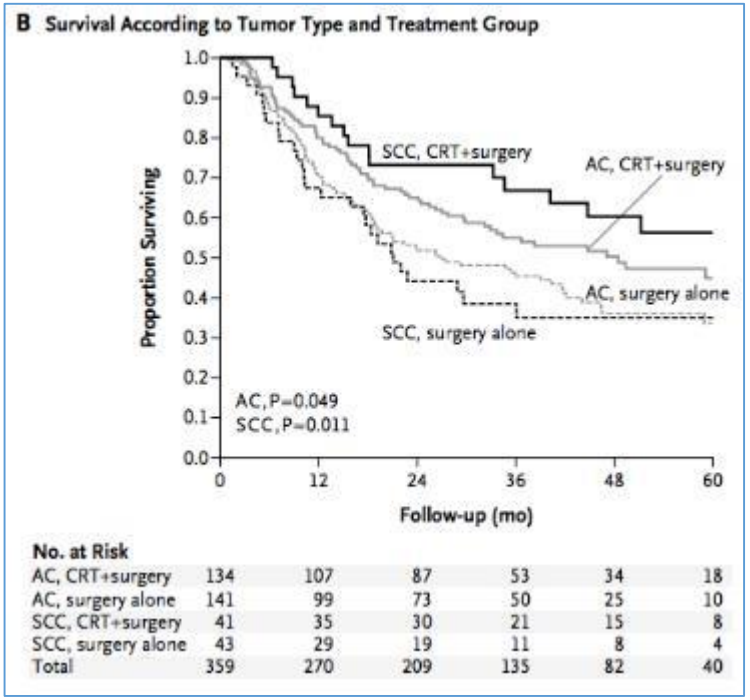
→

R0: CRT+S = **92%**
Surgery = **69%**

N Engl J Med 2012;366:2074-84.

Preop. CRT + Surg. vs. Surg. only





OS: Preop. CRT + Surg. = **49.4** months
Surg. only = **24.0** months

N Engl J Med 2012;366:2074-84.

Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial

Joel Shapiro, J Jan B van Lanschot, Maarten C C M Hulshof, Pieter van Hagen, Mark I van Berge Henegouwen, Bas P L Wijnhoven, Hanneke W M van Laarhoven, Grard A P Nieuwenhuijzen, Geke A P Hospers, Johannes J Bonenkamp, Miguel A Cuesta, Reinoud J B Blaisse, Olivier R C Busch, Fiebo J W ten Kate, Geert-Jan M Creemers, Cornelis J A Punt, John Th M Plukker, Henk M W Verheul, Ernst J Spillenaar Bilgen, Herman van Dekken, Maurice J C van der Sangen, Tom Rozema, Katharina Biermann, Jannet C Beukema, Anna H M Piet, Caroline M van Rij, Janny G Reinders, Hugo W Tilanus, Ewout W Steyerberg, Ate van der Gaast, for the CROSS study group

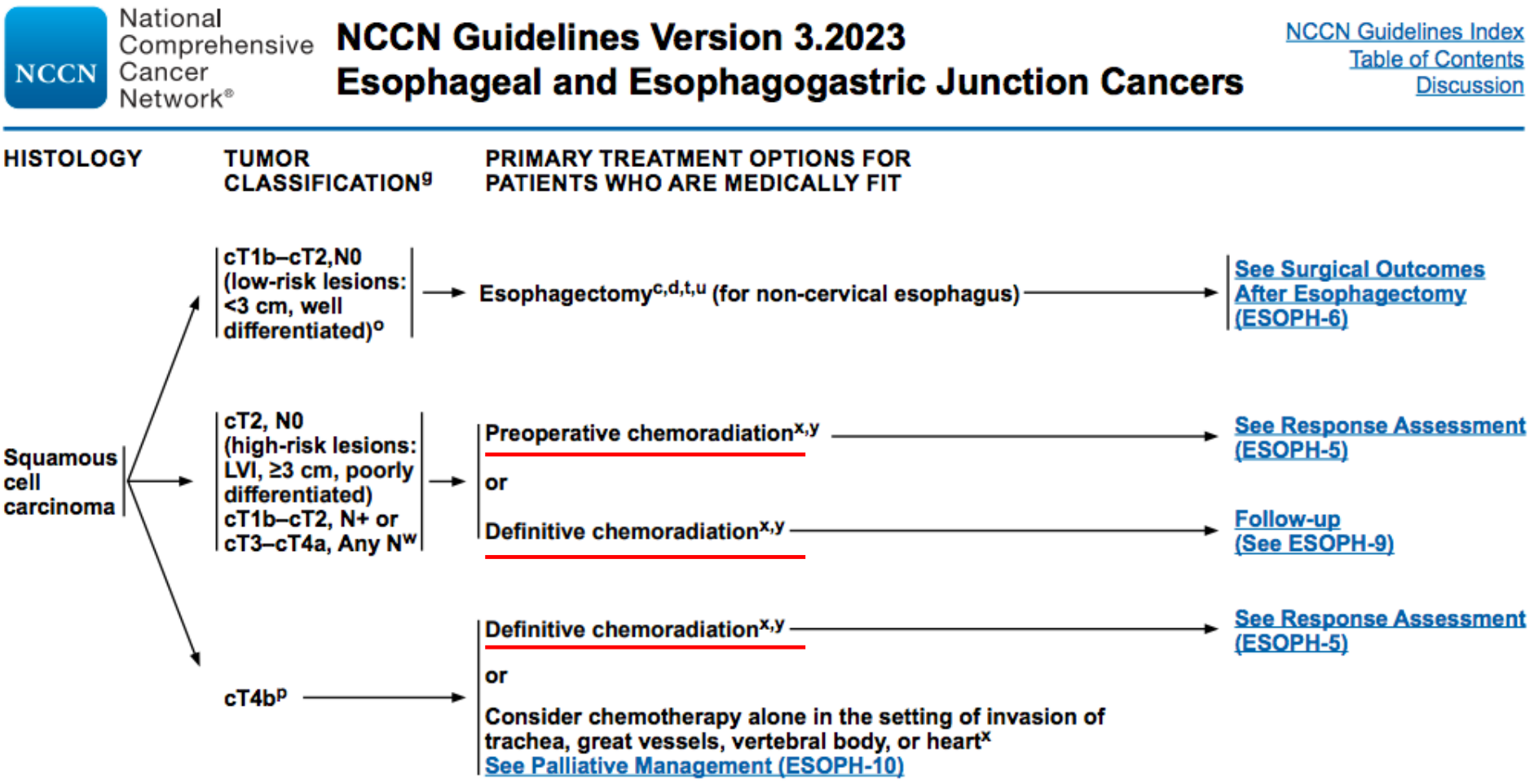
Long-term follow-up confirms the overall survival benefits for neoadjuvant chemoradiotherapy when added to surgery in patients with resectable oesophageal or oesophagogastric junctional cancer.

OS:

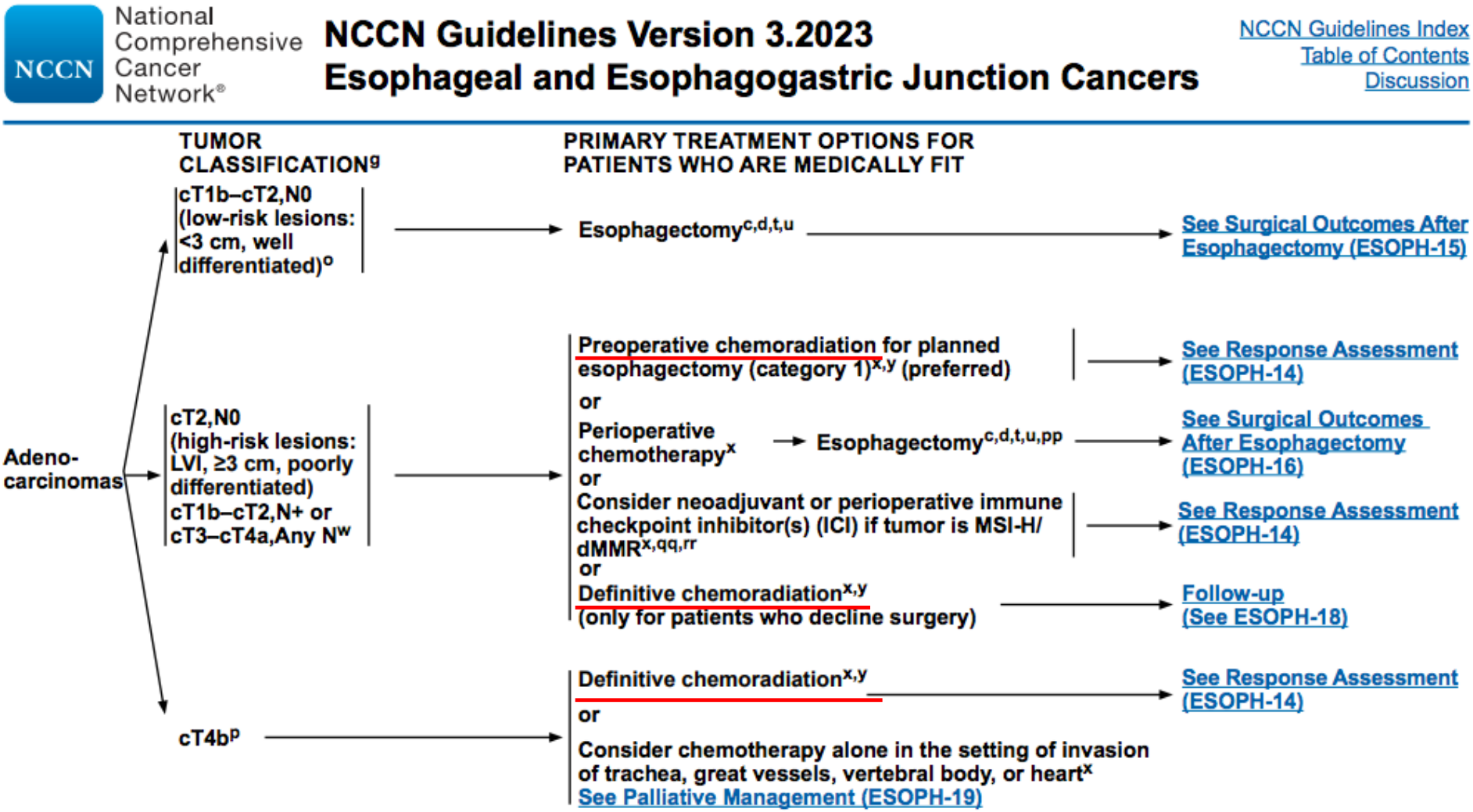
	CRT + Surg.	Surg. only
SCC	81.6 mon.	21.1 mon
ACA	43.2 mon.	27.1 mon

Lancet Oncol 2015; 16: 1090–98

Primary treatment options: SCC



Primary treatment options: ACA



Preoperative chemoradiation:

(more often)

RT 41.4-50.4Gy + concurent chemotherapy

Paclitaxel 50mg/m2 + Carboplatin AUC 2 weekly

NCCN 3.2023

Definitive chemoradiation:

(for locally advanced inoperable EC)

RT 50-50.4Gy + concurent chemotherapy

Cisplatin 75-100mg/m2
Fluorouracil 750-1000mg/m2 days 1-5

NCCN 3.2023

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2023
Esophageal and Esophagogastric Junction Cancers

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY
REFERENCES

[1] Lin SH, Hobbs BP, Verma V, et al. Randomized phase IIB trial of proton beam therapy versus intensity-modulated radiation therapy for locally advanced esophageal

Recommendations for dosing based on the INT 0123 trial (RTOG 9405), in which dose escalation from 50.4 to 64.8Gy did not increase OS

Minsky BD et al., J Clin Oncol. 2002;20(5):1167–1174.

Studies regarding high-dose RT and/or conventional-dose RT in esophageal

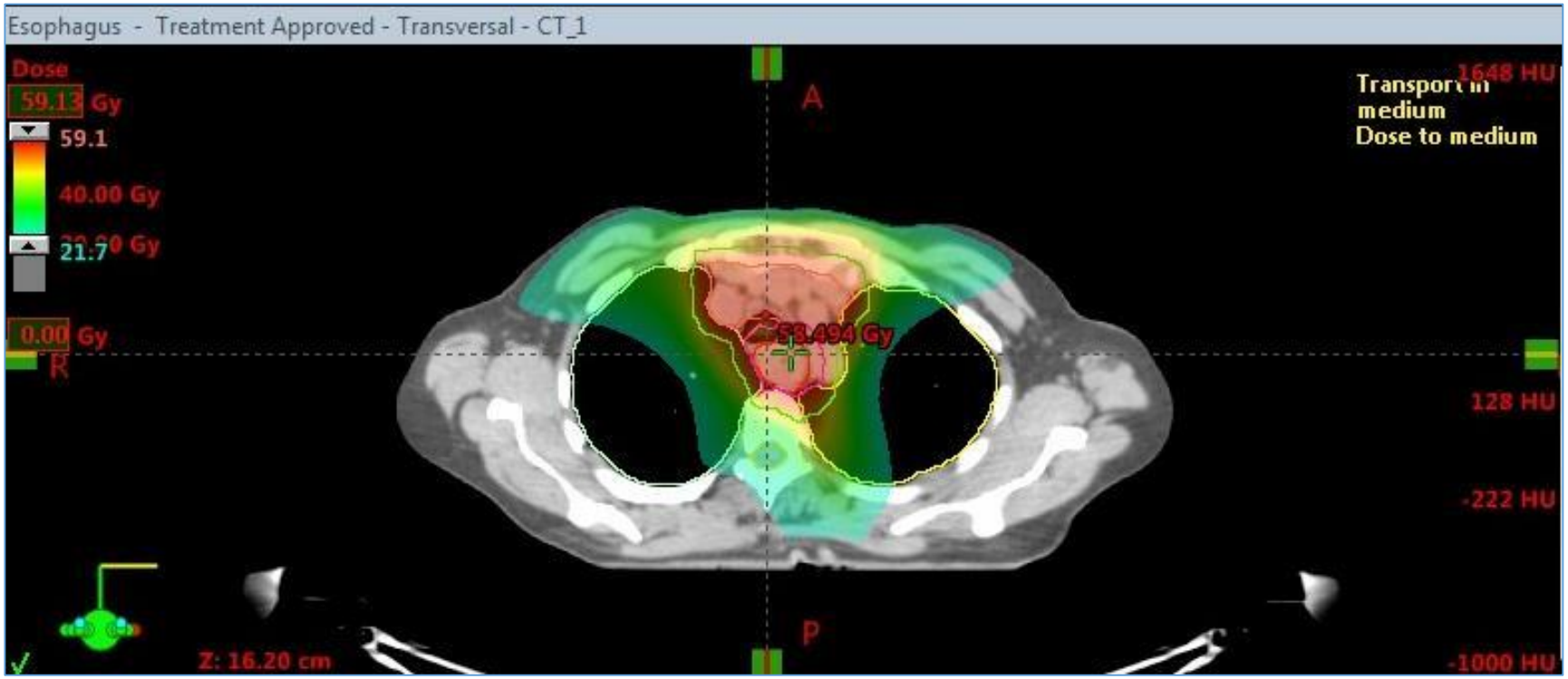
Table 1 Studies regarding high-dose RT and/or conventional-dose RT in esophageal cancer

Authors	Radiation dosage	Radiation technique	No. of patients	LCR, %	*p*-value	OS	*p*-value
Minsky et al[8]	50.4 Gy	2D-RT	109	52 (LFR)	>0.05	40% (2 year)	>0.05
	64.8 Gy		109	56		31%	
Zhang et al[29]	<51 Gy	2D-RT	43	19 (3 year)	0.011	3% (3 year)	0.054
	≥51 Gy		26	36		13%	
Suh et al[27]	<60 Gy	2D-RT	49	32 (2 year)	<0.01	18 months (MST)	0.26
	≥60 Gy		77	69		28 months	
He et al[28]	≤50.4 Gy	3D-RT	137	34.3 (LFR)	0.024	33.0% (5 year)	0.617
	>50.4 Gy		56	17.9		41.7%	
Kim et al[30]	<60 Gy	3D-RT or	120	37.3 (5 year)	0.02	22.3 months (MST)	0.043
	≥60 Gy	IMRT	116	59.7		35.1 months	
Chen et al[31]	50–50.5 Gy	3D-RT	324	NR	NR	14% (5 year)	<0.05
	≥60 Gy		324	NR		22%	
Chen et al[36]	GTV 66 Gy /30f	SIB-IMRT	60	78.6% (2 year)	–	72.7% (2 year)	–
	CTV 54 Gy/30f						

Abbreviations: CTV, clinical target volume; GTV, gross target volume; IMRT, intensity modulated radiotherapy; LCR, local control rate; LFR, local failure rate; MST, median survival time; NR, not reported; OS, overall survival; RT, radiotherapy; SIB, simultaneous integrated boost.

Luo et al., 2018

Case: a 65 year old woman, ESCC cT3N2M0
Upper and middle thirds of the esophagus



PET
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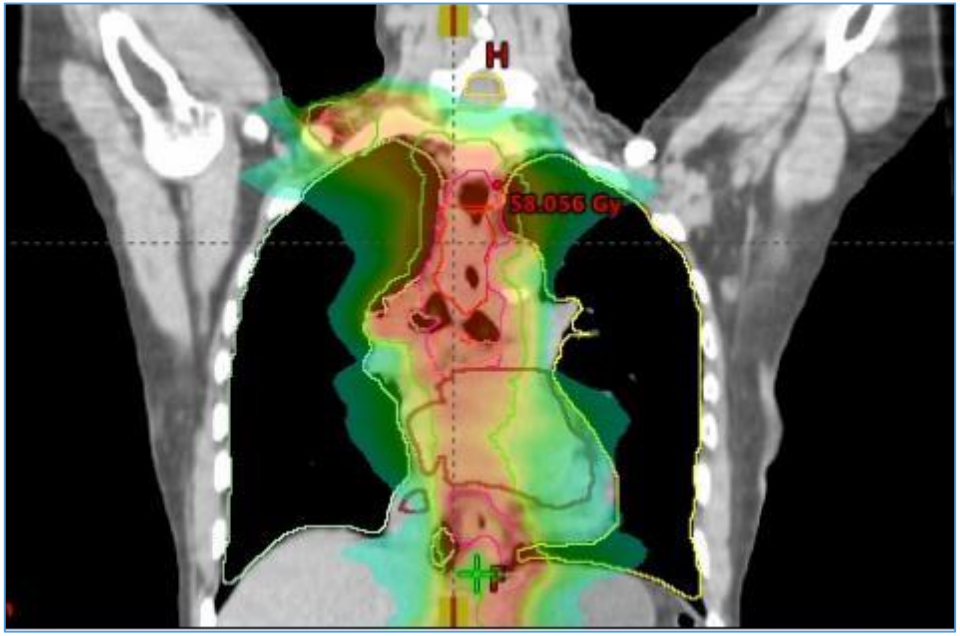
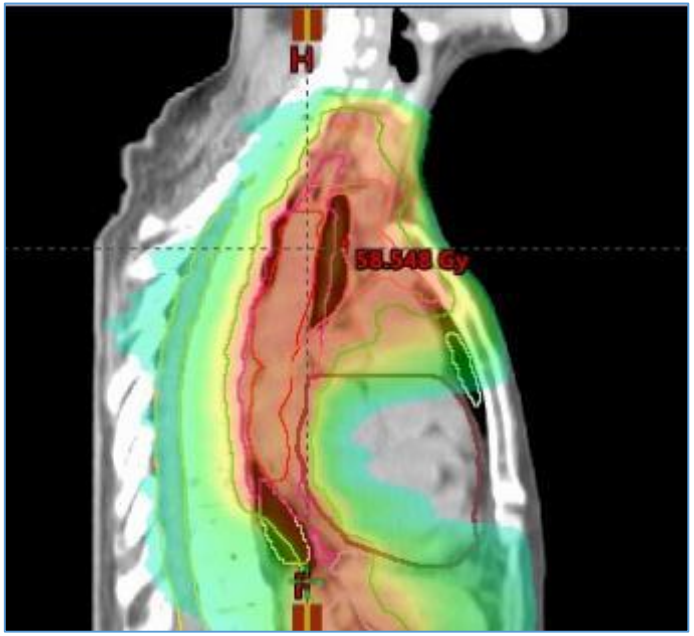
Case: a 65 year old woman, ESCC cT3N2M0
Upper and middle thirds of the esophagus

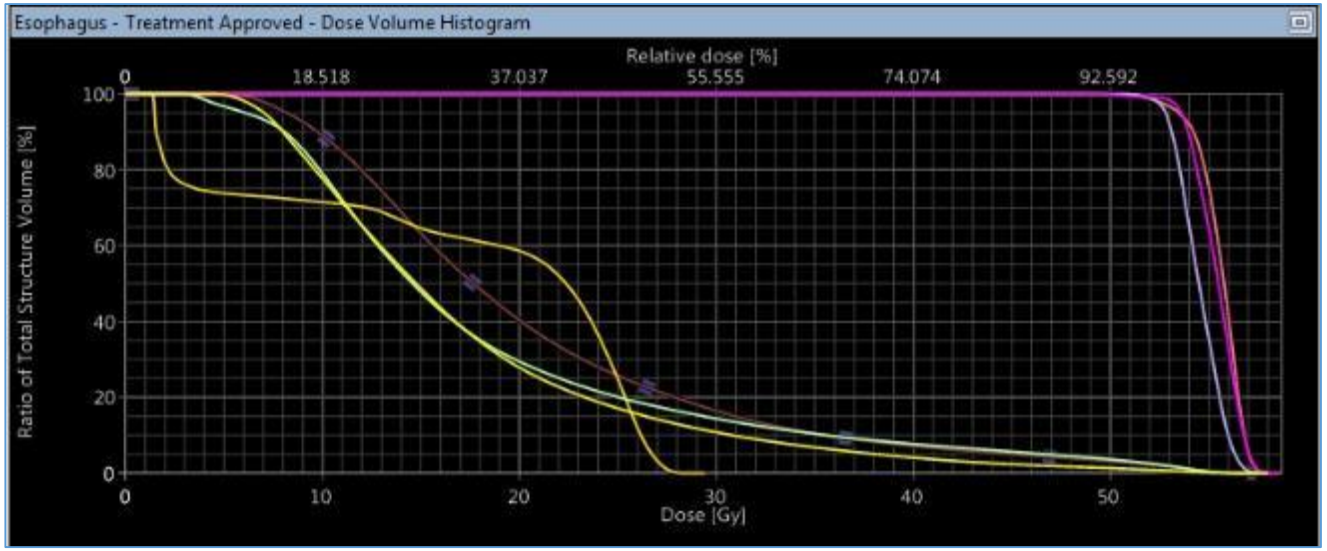


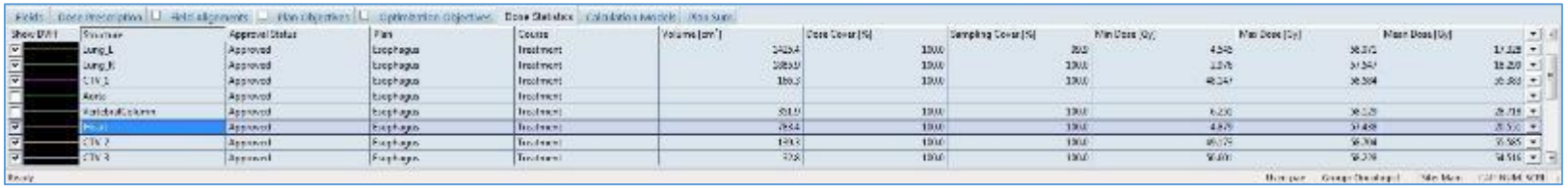


PET
Technology

Case: a 65 year old woman, ESCC cT3N2M0
Upper and middle thirds of the esophagus

VMAT 54 Gy + 5FU





PET
Technology

Conclusion

1. Preoperative chemoradiotherapy improved survival among patients with potentially curable esophageal cancer.

2. The standard RT dose (50.4 Gy in 28 fractions) may be inadequate to achieve a high probability for LC for some subgroup patients.

3. The some studies indicate that a higher radiation dose could improve local tumor control, and may also confer survival benefits.

4. The course of radiation therapy should be without interruptions.

Gastric cancer

Incidence

Highest: up to 69 cases per 100 000 people per year – in northeast Asia (**Japan, Korea, and China**)

Intermediate: in Europe and South America

Low: rates of 4–10 cases per 100 000 people - in North America, Africa, south Asia, and Oceania (including Australia and New Zealand)

Yamaoka Y, 2008

Gastric cancer

Surgical resection of the primary tumor and regional lymph nodes is the treatment of choice for gastric cancer.

Risk factors:

- Lymphatic, venous, or perineural invasion
- Positive surgical resection margin
- Lesion in the whole stomach
- Large number positive lymph. nodes
- Lymph node dissection < then D2

Surgery plus chemoradiotherapy vs Surgery only

CHEMORADIOTHERAPY AFTER SURGERY COMPARED WITH SURGERY ALONE FOR ADENOCARCINOMA OF THE STOMACH OR GASTROESOPHAGEAL JUNCTION

JOHN S. MACDONALD, M.D., STEPHEN R. SMALLEY, M.D., JACQUELINE BENEDETTI, PH.D., SCOTT A. HUNDAHL, M.D., NORMAN C. ESTES, M.D., GRANT N. STEMMERMANN, M.D., DANIEL G. HALLER, M.D., JAFFER A. AJANI, M.D., LEONARD L. GUNDERSON, M.D., J. MILBURN JESSUP, M.D., AND JAMES A. MARTENSON, M.D.

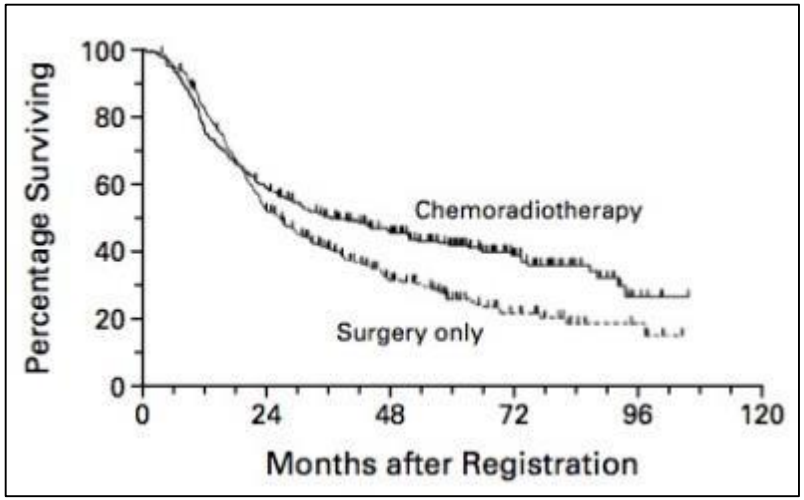
556 patients – total (adenocarcinoma):
275 pts. – surgery only
281 pts. – surgery plus chemoradiotherapy

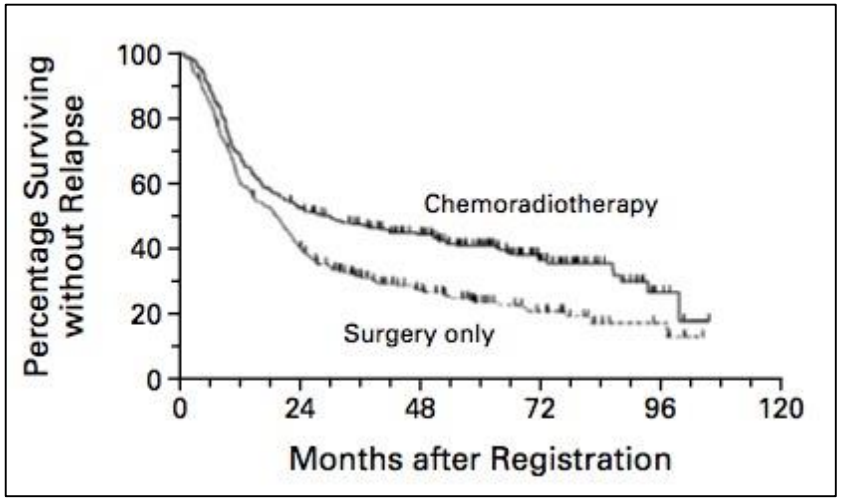
T1-4; N0-3

CRT: 45Gy/25fr. + { fluorouracil 400mg/m2; leucovorin 20mg/m2

N Engl J Med, Vol. 345, 2001

Results





OS

Surgery – 27 mon.

S.+ CRT – 36 mon.

RFS

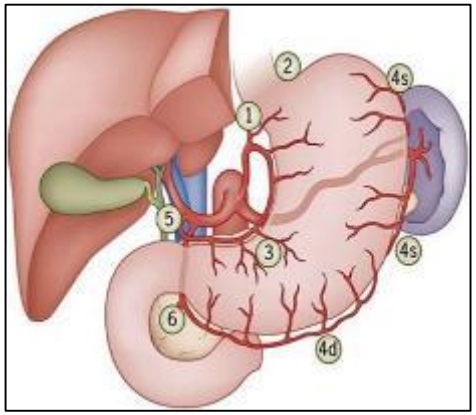
Surgery – 19 mon.

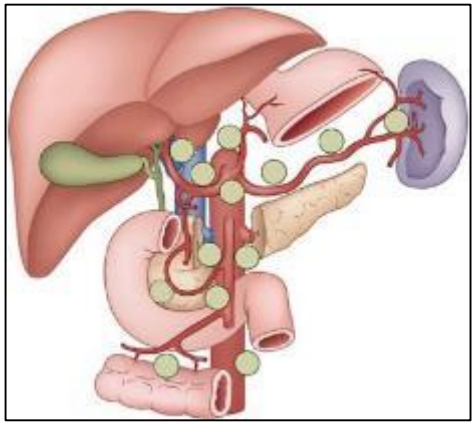
S.+ CRT – 30 mon.

for all stages

N Engl J Med, Vol. 345, 2001

Lymph Nodes Groups Surrounding the Stomach



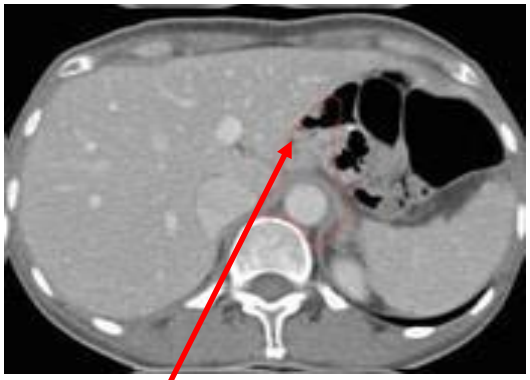


1. Right cardial nodes
2. Left cardial nodes
3. Nodes along the lesser curvature
4. Nodes along the greater curvature
5. Suprapyloric nodes
6. Infrapyloric nodes
7. Nodes along left gastric artery
8. Nodes along the common hepatic artery
9. Nodes along the celiac axis
10. Nodes at the splenic hilus
11. Nodes along the splenic artery
12. Nodes in the hepatoduodenal ligament
13. Nodes at the posterior aspect of pancreatic head
14. Nodes at the root of the mesenterium
15. Nodes in the mesocolon of the transverse colon
16. Para-aortic lymph nodes

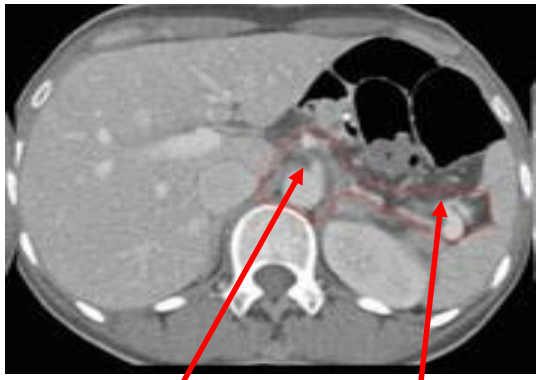
Hartgrink HH, 2005

CTV for **T1N1M0** adenocarcinoma of the gastric cardia post-total gastrectomy

Coverage of esophagojenunal anastomosis



Coverage of hepatogastric ligament

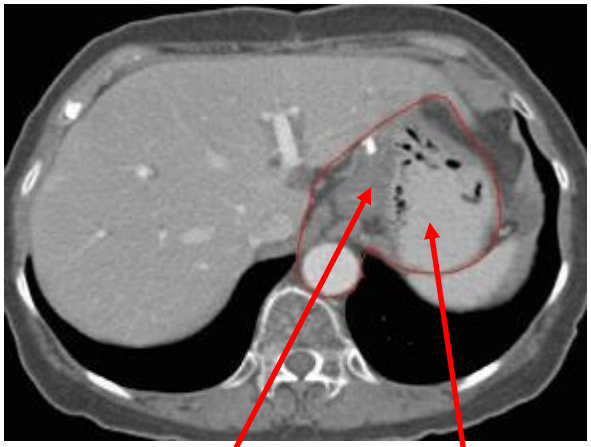


Coverage of celiac artery

Coverage of splenic hilum

N.Y.Lee, 2013

CTV of **T3N3M0** adenocarcinoma of the gastric body post-distal gastrectomy



Coverage of gastrojejunal anastomosis

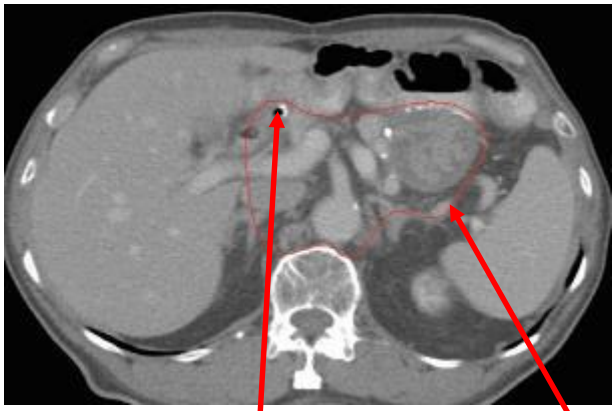
Coverage of remnant stomach

Coverage of Celiac artery

Coverage of splenic hilum

N.Y.Lee, 2013

CTV of **T2N1M0** adenocarcinoma of the antrum/pylorus post-distal gastrectomy



Coverage of hepatogastric ligament, gastrojejunal anastomosis

Coverage of remnant stomach

Coverage of duodenal stump

Optional coverage of splenic hilum

N.Y.Lee, 2013

Radiotherapy

RT Dosing (1.8Gy/d):
R0: 45-50.4 Gy
R1-2: 59.4-61.2 Gy
(boost)

Empty Stomach

Dose constraints:

Lung V20Gy<30%, Dmean<20Gy;
Heart V30Gy<30%, Dmean<30%;
Kidney V20Gy<33%, Dmean<18Gy;
Liver V30Gy <33%, Dmean<25Gy;
Bowel V45Gy<195cc;
Spinal cord Dmax<45Gy.

Lymph nodes:

Proximal 1/3: perigastric, celiac, left gastric artery, splenic artery, splenic hilar, hepatic artery, and porta hepatic lymph nodes.

Middle 1/3: perigastric, celiac, left gastric artery, splenic artery, splenic hilar, hepatic artery, porta hepatic, suprapyloric, subpyloric, and pancreaticoduodenal lymph nodes.

Distal 1/3: perigastric, left gastric artery, celiac, hepatic artery, porta hepatic, suprapyloric, subpyloric, and pancreaticoduodenal lymph nodes.

Tepper JE, Gunderson LE, 2002

Conclusion

Postoperative chemoradiotherapy should be considered for all patients at high risk for recurrence of adenocarcinoma of the stomach or gastroesophageal junction who have undergone curative resection.

Rectal cancer

Current standard of neoadjuvant treatment for locally advanced rectal cancer (cT3-4 and/or cN+) is either the use of preoperative short-course radiotherapy (5 x 5 Gy) or preoperative, conventionally fractionated radiotherapy with oral capecitabine or continuous infusion 5-FU, followed by total mesorectal excision surgery six weeks there after.

Randomized trials

Trial	Design	Results
Polish, fase 3	5x5Gy + FOFOX4 (№3) vs Long-course 50.4Gy CRT	No differences. SCRT: lower acute toxicity
STELLAR, fase 3	5x5Gy + CAPOX (№4) vs Long-course 50Gy CRT	No differences
RAPIDO, fase 3	5x5Gy + CAPOX (№6) vs Long-course 50Gy CRT	Toxicity ≥grade 3 occurred in 48% of SCRT, compared to 25% in the standard arm

Bujko K, 2016
Jin J, 2022
van der Valk, 2020

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 0: 1–6, 2019
doi:10.1093/annonc/mdz186
Published online 13 June 2019

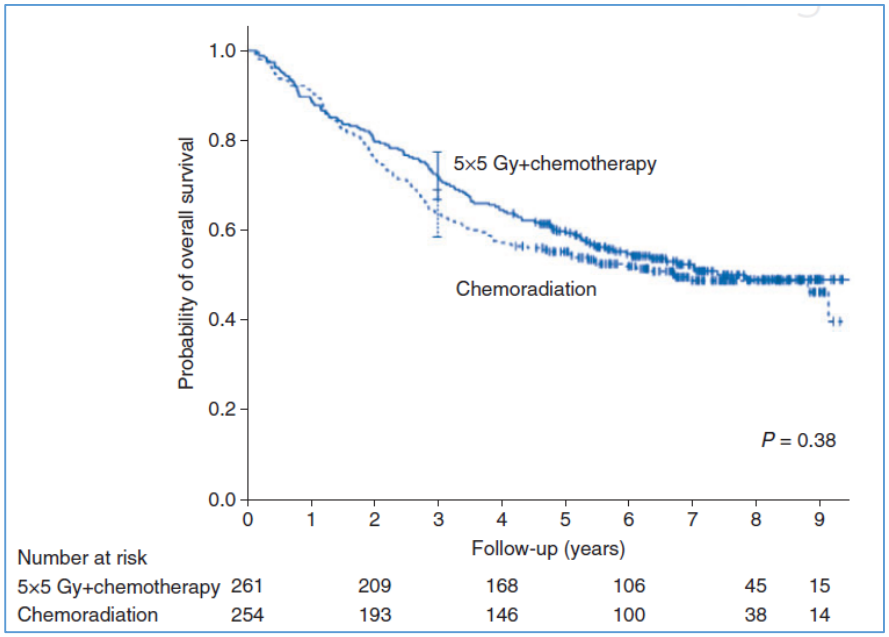
ORIGINAL ARTICLE

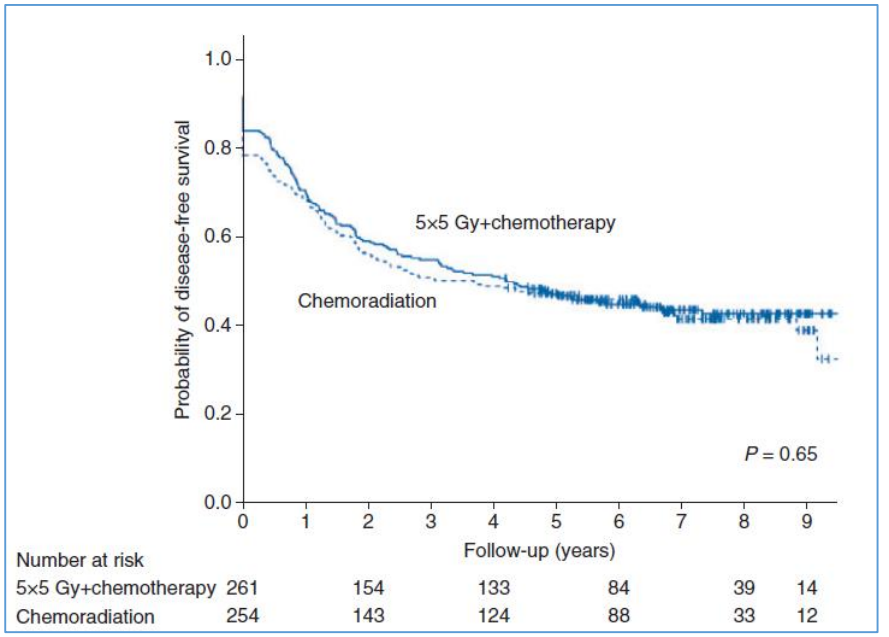
Long-course preoperative chemoradiation versus 5 × 5 Gy and consolidation chemotherapy for clinical T4 and fixed clinical T3 rectal cancer: long-term results of the randomized Polish II study

B. Ciseł[1], L. Pietrzak[2], W. Michalski[3], L. Wyrwicz[4], A. Rutkowski[5], E. Kosakowska[5], A. Cencelewicz[5], M. Spałek[2], W. Polkowski[1], M. Jankiewicz[1,6], R. Styliński[7], M. Bębenek[8], B. Kapturkiewicz[8], A. Maciejczyk[9], J. Sadowski[10], J. Zygulska[11], W. Zegarski[12], M. Jankowski[12], M. Las-Jankowska[13], Z. Toczko[14], U. Żelazowska-Omiotek[15], L. Kępka[16], J. Socha[16,17], E. Wasilewska-Tesluk[18,19], W. Markiewicz[20], J. Kładny[21], A. Majewski[22], W. Kapuściński[23], R. Suwiński[24] & K. Bujko[2*], for the Polish Colorectal Study Group

515 patients
261 in the short-course/CCT
254 in the chemoradiation

Long-course vs 5x5 Gy

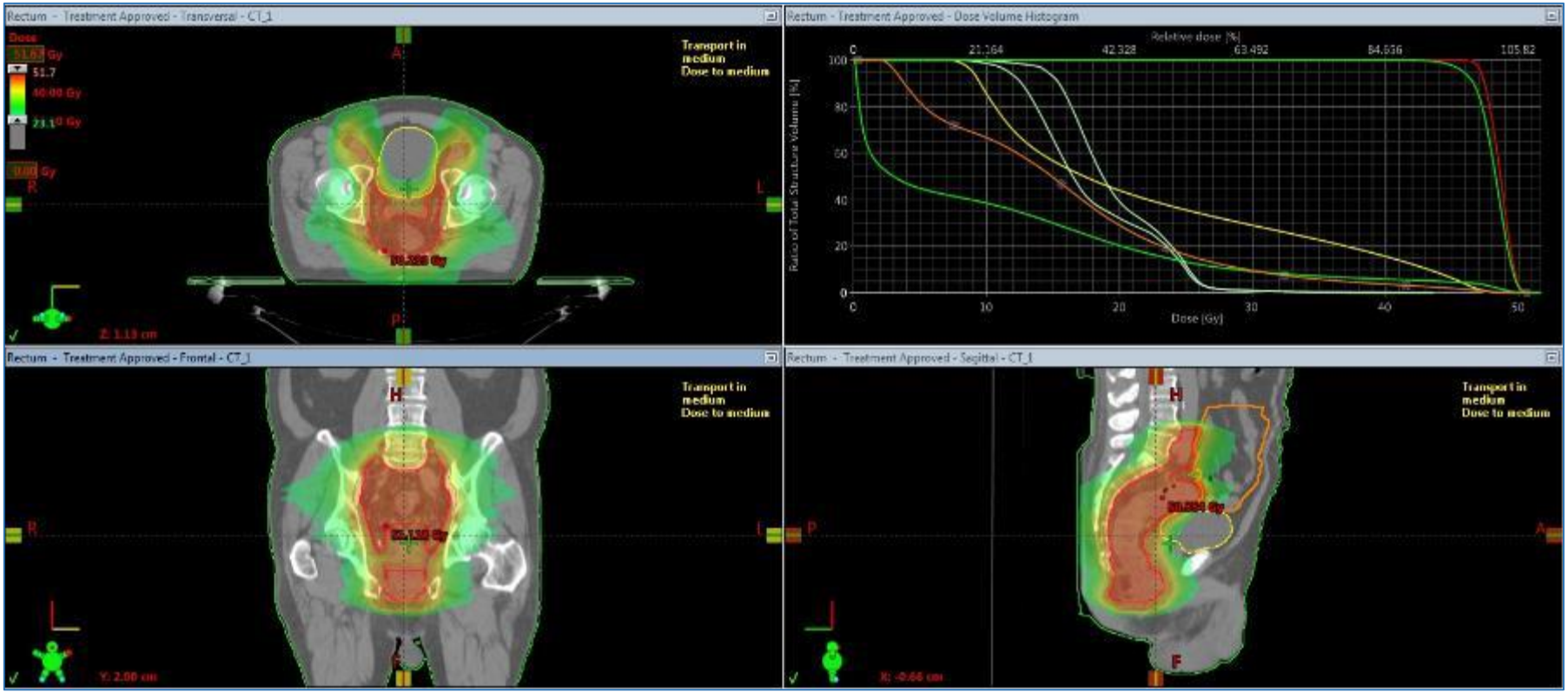




The superiority of preoperative short-course/CCT over chemoradiation was not demonstrated.

Annals of Oncology 0: 1–6, 2019

Case: men 56 y.o., AC cT3N1M0



PET
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Conclusion

SCRT with immediate or delayed surgery is as effective as LCRT with delayed surgery for treatment of rectal cancer in terms of OS, DFS, LRR, Sphincter preservation rate, R0 resection rate and late toxicity.

Though LCRT increased pathologic complete response (pCR) rate, LCRT also increased acute toxicity compared with SCRT.

SCRT is a better choice in centers with a long waiting list or lack of medical resources.

Thank you so much!